Complementary Therapies in Medicine (2013) 21, 164—171

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The clinical efficacy of a bovine lactoferrin/whey protein Ig-rich fraction (Lf/IgF) for the common cold: A double blind randomized study

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Available online 8 January 2013

KEYWORDS
Bovine lactoferrin;
Whey protein immunoglobulins;
Clinical efficacy;
Common cold

Summary
Objective: The aim of the study was to determine if a bovine lactoferrin/whey protein Ig-rich fraction (Lf/IgF) combination was effective in reducing the number of colds and in turn improving symptom recovery in a cohort of males and females that reported frequently contracting a cold.
Design: A double blind randomized placebo-controlled clinical trial.
Setting: One-hundred and twenty-six participants matched by age, BMI, dietary and physical parameters with self-reported frequent upper respiratory tract symptoms and infections were randomly assigned to receive 600 mg of Lf/IgF or a placebo daily for 90 days.
Main outcome measures and results: A total of 90 participants (47 receiving the active and 43 placebo) completed the 90 day trial and 15 completed 45 days participation (6 in the active and 9 in the placebo group). The total number of colds recorded over the study period was 48 for the treatment group versus 112 for the placebo group ($p < 0.001$). The significant trend was retained when the data was corrected for medications returned ($p < 0.001$) and for guessing treatment allocations ($p < 0.001$). Non-parametric analysis demonstrated that the total number of cold-associated symptoms reported by participants that received Lf/IgF was significantly less than those in the placebo group ($p < 0.05$). Also, total days sick with a cold and cold severity were reduced over the clinical trial period for Lf/IgF over placebo, but the trend was not significant.
Conclusions: These findings demonstrate that the Lf/IgF combination significantly decreased the incidence of colds and the cumulative number of cold-related symptoms over placebo. This therapeutic combination may be indicated for the prevention of colds and its most common symptoms in the general population when administered as a preventative supplement.

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http://dx.doi.org/10.1016/j.ctim.2012.12.006

Introduction

Acute respiratory tract illnesses and acute upper respiratory tract infections (URTIs), traditionally referred to as common colds, are the most prevalent diseases experienced by the community. It is a leading cause of doctor visits, accounting for more days off work or school and limited activity than any other acute illness.[1] Mechanisms that spread cold viruses include aerosol particles and direct contact, however regardless of the mechanism, contact between the virus and nasal mucosa appears to be important for initiation of infection.[1] More than 200 viruses are known to cause the common cold with rhinoviruses accounting for 30—50% of all adult related colds.[2,3] The viral mutations and self-limiting aspects of the common cold and associated complications make effective treatment options difficult and the development of additional therapeutic modalities limited in efficacy.

Conventional goals of treatment for cold-associated viruses include amelioration of the symptoms of the illness, prevention of person-to-person spread of infection and prevention of the complications of the common cold (i.e. otitis media, sinusitis and exacerbations of reactive airway disease). Current treatments available are limited to symptomatic therapies such as acetaminophen (paracetamol), codeine and various decongestants as the analgesics of choice in relation to safety profiles. Interest by the community in nutraceutical-based therapies has increased over the last decade in an attempt to address the perceived therapeutic deficits that exist with URTI preventions and treatments. Natural compounds used include vitamins [e.g. vitamin C], minerals [e.g. zinc] and herbal compounds such as *Echinacea* and Garlic.[4—8] Recent research has also provided biologically plausible mechanisms by which lactoferrin (Lf) a natural component of most exocrine biological fluids [i.e. tears, saliva, nasal and bronchial secretions, gastrointestinal fluids, colostrum and particularly breast milk] may provide a potential prophylactic solution to the common cold.[9—11] Lf is an iron-binding glycoprotein that is part of the transferrin protein family and is also a major component of the secondary granules of neutrophils released into serum at inflammatory sites.[9]

Whey protein, a high-biologic-value protein with immunoglobulin's composing part of its major protein fractions, has also been demonstrated to enhance the immune system and has been reported to exhibit antimicrobial and antiviral activity.[12—14] A recent clinical trial utilising a high dose of whey protein [40 g/day] demonstrated immune function efficacy in Human Immunodeficiency Virus participants, with significant increased CD4 cell counts.[15]

Hence, the rationale for the current clinical trial investigation was based on published studies that demonstrate Lf combined with whey protein may provide an efficacious therapeutic option for preventing and or treating the common cold. The trial was designed to evaluate the efficacy and further safety of a commercially available dietary supplement, comprising a combination of Lf and IgF from bovine whey protein, in the prevention and reduction in time of symptom recovery from infections that cause the common cold.

Methods

All participants gave written consent prior to their participation in the clinical trial. The randomization for the clinical study design involved generating one randomization list [independently generated by non-investigators] at the start of the trial that was double-blinded to participants and research/recruitment personnel. The allocation sequence was concealed and the treatment ratio was 1:1. Participants were recruited from the local Brisbane area in response to advertisements in local papers and advertisements placed in the Princess Alexandra Hospital from January 2008 until March 2010. Participants were initially pre-screened via a telephone interview followed by a face—face baseline screening [visit 1] at the Princess Alexandra Hospital in Brisbane in a dedicated clinical trial facility. Follow-up visits, visit 2 at 45 days and visit 3 at 90 days, was conducted at the same location.

The *inclusion criteria* included participants to be 18 years or older and to frequently experience two or more cold-associated symptoms that lasted $\geq$2 days (i.e. cough, nasal congestion, sore throat, watery eyes, runny nose, itchy nose, throat or eyes, headaches and fatigue) in the previous 6 months (at least 3 common cold events) to be eligible to proceed to the next phase of induction. Additional inclusion criteria included general good health and female participants agreeing to continue adopting birth control measures for the duration of the trial. The *exclusion criteria* included the current or recent [within the last month] use of all natural supplements including vitamins and minerals, herbal preparations and probiotics. Participants who were pregnant or lactating, unwilling to adhere to the study protocol, had a history of alcohol or substance abuse, or had a history of serious or unstable cardiac, renal, hypertensive, pulmonary, endocrine, immunologic, neurologic or neuropsychiatric disorders were ineligible to participate. Furthermore, participants were asked and agreed to abstain from commercial products containing vitamins, minerals, herbs, fish oils or probiotics for the duration of the trial. Prospective participants who chose to stop the use of natural supplements were considered for inclusion after a one-month wash-out period.

Eligible participants were randomized and allocated to either the treatment supplement of Lf (200 mg)/IgF (100 mg) [2 $\times$ 300 mg/cap daily] or placebo [2 $\times$ 300 mg/cap daily of calcium phosphate] for a total of 90 days. Participants who satisfied the inclusion and exclusion criteria were provided with a diary (at baseline visit 1 and at 45 days visit 2) to record any common cold symptoms experienced during the 90-day trial. The diary had listed all the common cold symptoms that a participant may experience facilitating proper recording of cold associated symptoms. The symptoms of the common cold included sore throat, nasal congestion, sinus swelling, sneezing, cough, headache and fatigue.[4] The diary was constructed to record symptom duration and severity and the incidence of any other acute illness experienced during the trial period.

On induction into the clinical trial [baseline visit 1], participants were carefully instructed to record any cold related symptoms or changes in their health over the proceeding 45 days in the event diary noting symptom